

SEQUENCE LISTING

<110> Horvitz, H. Robert Yuan, Junying Shaham, Shai

<120> Relatedness of Human Interleukin-1beta Convertase Gene to a C. Elegans Cell Death Gene, Inhibitory Portions of these Genes and Uses Therefor

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Met Met Arg Gln Asp Arg Trp Leu Leu Glu Arg Asn Ile Leu Glu Phe 10 Ser Ser Lys Leu Gln Ala Asp Leu Ile Leu Asp Val Leu Ile Ala Lys 20 Gln Val Leu Asn Ser Asp Asn Gly Asp Val Ile Asn Ser Cys Arg Thr 40 Glu Arg Asp Asn Glu Lys Glu Ile Val Lys Ala Val Gln Arg Arg Gly 55 Asp Glu Ala Phe Asp Ala Phe Tyr Asp Ala Leu Arg Asp Thr Gly His 70 Asn Asp Leu Ala Asp Val Leu Met Pro Leu Ser Arg Pro Xaa Xaa Xaa Asn Pro Val Pro Met Glu Cys Pro Met Ser Pro Ser Ser His Arg Arg 100 105 Ser Arg Ala Leu Ser Pro Pro Xaa Tyr Ala Ser Pro Thr Arg Val His 115 120 Arg Asp Ser Ile Ser Ser Val Ser Ser Phe Thr Ser Thr Tyr Gln Asp 135 140 Val Tyr Ser Arg Ala Arg Ser Ser Ser Arg Ser Ser Pro Leu Gln 150 155 Ser Ser Asp Arg His Asn Tyr Met Ser Ala Ala Thr Ser Phe Pro Ser 165 170 Gln Pro Xaa Ser Ala Asn Ser Ser Phe Thr Gly Cys Ala Ser Leu Gly 180 185 Tyr Ser Ser Ser Arg Asn Arg Ser Phe Ser Lys Thr Ser Ala Gln Ser 200 205 Gln Tyr Ile Phe His Glu Glu Asp Met Asn Tyr Val Asp Ala Pro Thr 215 220 Ile His Arg Val Phe Asp Glu Lys Thr Met Tyr Arg Asn Phe Ser Ser

230 235 Pro Arg Gly Leu Cys Leu Ile Ile Asn Asn Glu His Phe Glu Gln Met 245 250 Pro Thr Arg Asn Gly Thr Lys Ala Asp Lys Asp Asn Leu Thr Asn Ile 265 260 270 Phe Arg Cys Met Gly Tyr Thr Val Ile Cys Lys Asp Asn Leu Thr Gly 275 280 285 Arg Glu Met Leu Ser Thr Ile Arg Ser Phe Gly Arg Asn Asp Met His 295 300 Gly Asp Ser Ala Ile Leu Val Ile Leu Ser His Gly Glu Xaa Asn Val 310 315 Ile Ile Gly Val Asp Asp Val Ser Val Asn Val His Glu Ile Tyr Asp 325 330 Leu Leu Asn Ala Ala Asn Ala Pro Arg Leu Ala Asn Lys Pro Lys Leu 345 Val Phe Val Gln Ala Cys Arg Gly Glu Arg Arg Asp Asn Gly Phe Pro 360 Val Leu Asp Ser Val Asp Gly Val Pro Ser Leu Ile Arg Arg Gly Trp 375 380 Asp Asn Arg Asp Gly Pro Leu Phe Asn Phe Leu Gly Cys Val Arg Pro 390 395 Gln Val Gln Gln Val Trp Arg Lys Pro Ser Gln Ala Asp Met Leu 405 410 Ile Ala Tyr Ala Thr Thr Ala Gln Tyr Val Ser Trp Arg Asn Ser Ala 425 430 Arg Gly Ser Trp Phe Ile Gln Ala Val Cys Glu Val Phe Ser Leu His 440 Ala Lys Asp Met Asp Val Val Glu Leu Leu Thr Glu Val Asn Lys Lys 455 Val Ala Cys Gly Phe Gln Thr Ser Gln Gly Ser Asn Ile Leu Lys Gln 470 475 Met Pro Glu Leu Thr Ser Arg Leu Leu Lys Lys Phe Tyr Phe Trp Pro 490 485 Glu Asp Arg Gly Arg Asn Ser Ala Val 500

<210> 6 <211> 479 <212> PRT

<213> Caenorhabditis vulgaris

<220>

<221> VARIANT

<222> 98, 292, 310

<223> Xaa = Any Amino Acid

<400> 6

90 85 Pro Xaa Tyr Ala Ser Pro Thr Arg Val His Arg Asp Ser Ile Ser Ser 105 100 Val Ser Ser Phe Thr Ser Thr Tyr Gln Asp Val Tyr Ser Arg Ala Thr 115 120 125 Ser Ser Ser Pro Leu Gln Thr Ser Asp Arg His Asn Tyr Val Ser Ala 140 135 Ser Thr Ser Phe Gln Ser Gln Pro Ala Ser Ala Asn Ser Ser Phe Thr 150 155 Gly Ser Ala Ser Leu Gly Tyr Ser Ser Ser Arg Thr Arg Ser Tyr Ser 165 170 Lys Thr Ser Ala His Ser Gln Tyr Ile Phe His Glu Glu Asp Met Asn 185 Tyr Val Asp Ala Pro Thr Ile His Arg Val Phe Asp Glu Lys Thr Met 200 Tyr Arg Asn Phe Ser Thr Pro Arg Gly Leu Cys Leu Ile Ile Asn Asn 215 Glu His Phe Glu Gln Met Pro Thr Arg Asn Gly Thr Lys Pro Asp Lys 230 235 Asp Asn Ile Ser Asn Ile Phe Arg Cys Met Gly Tyr Ile Val His Cys 250 245 Lys Asp Asn Leu Thr Gly Arg Glu Met Met Ser Thr Ile Arg Ser Phe 270 260 265 Gly Arg Asn Asp Thr His Gly Asp Ser Ala Ile Leu Val Ile Leu Ser 275 285 280 His Gly Glu Xaa Asn Val Ile Ile Gly Val Asp Asp Val Ser Val Asn 295 300 Val His Glu Ile Tyr Xaa Leu Leu Asn Ala Ala Asn Ala Pro Arg Leu 310 315 Ala Asn Lys Pro Lys Leu Val Phe Val Gln Ala Cys Arg Gly Glu Arg 325 330 Arg Asp Val Gly Phe Pro Val Leu Asp Ser Val Asp Gly Val Pro Ser 345 Leu Ile Arg Arg Gly Trp Asp Lys Gly Asp Gly Pro Leu Phe Asn Phe 360 Leu Gly Cys Val Arg Pro Gln Ala Gln Gln Val Trp Arg Lys Lys Pro 375 380 Ser Gln Ala Asp Met Leu Ile Ala Tyr Ala Thr Thr Ala Gln Tyr Val 390 395 Ser Trp Arg Asn Ser Ala Arg Gly Ser Trp Phe Ile Gln Ala Val Cys 405 410 Glu Val Phe Ser Leu His Ala Lys Asp Met Asp Val Val Glu Leu Leu 420 425 430 Thr Glu Val Asn Lys Lys Val Ala Cys Gly Phe Gln Thr Ser Gln Gly 440 Ala Asn Ile Leu Lys Gln Met Pro Glu Leu Thr Ser Arg Leu Leu Lys 455 460 Lys Phe Tyr Phe Trp Pro Glu Asp Arg Asn Arg Ser Ser Ala Val

<210> 7

<211> 30

<212> DNA

<213> Artificial Sequence

<220>

<223> Synthetic Primer

<400> 7 tcatcgactt ttagatgact agagaacatc	30
<210> 8 <211> 30 <212> DNA <213> Artificial Sequence	
<220> <223> Synthetic Primer	
<400> 8 gttgcactgc tttcacgatc tcccgtctct	30
<210> 9 <211> 21 <212> DNA <213> Artificial Sequence	
<220> <223> Synthetic Primer	
<400> 9 gtttaattac ccaagtttga g	21
<210> 10 <211> 21 <212> DNA <213> Artificial Sequence	
<220> <223> Synthetic Primer	
<400> 10 ggttttaacc agttactcaa g	21
<210> 11 <211> 19 <212> DNA <213> Artificial Sequence	
<220> <223> Synthetic Primer	
<400> 11 ccggtgacat tggacactc	19
<210> 12 <211> 15 <212> DNA <213> Artificial Sequence	
<220> <223> Synthetic Primer	
<400> 12 actattcaac acttg	15
<210> 13	

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<211> 171
<212> PRT
<213> Murine
<220>
<221> VARIANT
<222> 117
<223> Xaa = Ala or Val
<400> 13
Met Leu Thr Val Gln Val Tyr Arg Thr Ser Gln Lys Cys Ser Ser Ser
                                    1.0
Lys His Val Val Glu Val Leu Leu Asp Pro Leu Gly Thr Ser Phe Cys
            2.0
                                25
Ser Leu Leu Pro Pro Pro Leu Leu Leu Tyr Glu Thr Asp Arg Gly Val
                            40
Asp Gln Gln Asp Gly Lys Asn His Thr Gln Ser Pro Gly Cys Glu Glu
                        55
Ser Asp Ala Gly Lys Glu Glu Leu Met Lys Met Arg Leu Pro Thr Arg
Ser Asp Met Ile Cys Gly Tyr Ala Cys Leu Lys Gly Asn Ala Ala Met
                85
Arg Asn Thr Lys Arg Gly Ser Trp Tyr Ile Glu Ala Leu Thr Gln Val
                                105
            100
Phe Ser Glu Arg Xaa Cys Asp Met His Val Ala Asp Met Leu Val Lys
                                                125
                            120
        115
Val Asn Ala Leu Ile Lys Glu Arg Glu Gly Tyr Ala Pro Gly Thr Glu
                                            140
                        135
Phe His Arg Cys Lys Glu Met Ser Glu Tyr Cys Ser Thr Leu Cys Gln
                    150
                                        155
Gln Leu Tyr Leu Phe Pro Gly Tyr Pro Pro Thr
                165
<210> 14
<211> 402
<212> PRT
<213> Murine
<400> 14
Met Ala Asp Lys Ile Leu Arg Ala Lys Arg Lys Gln Phe Ile Asn Ser
                                    10
Val Ser Ile Gly Thr Ile Asn Gly Leu Leu Asp Glu Leu Leu Glu Lys
           20
                                25
Arg Val Leu Asn Gln Glu Glu Met Asp Lys Ile Lys Leu Ala Asn Ile
                            40
Thr Ala Met Asp Lys Ala Arg Asp Leu Cys Asp His Val Ser Lys Lys
                        55
                                            60
Gly Pro Gln Ala Ser Gln Ile Phe Ile Thr Tyr Ile Cys Asn Glu Asp
                    70
                                        75
Cys Tyr Leu Ala Gly Ile Leu Glu Leu Gln Ser Ala Pro Ser Ala Glu
                                    90
Thr Phe Val Ala Thr Glu Asp Ser Lys Gly Gly His Pro Ser Ser Ser
                                105
```

Glu Thr Lys Glu Glu Gln Asn Lys Glu Asp Gly Thr Phe Pro Gly Leu 115 120 125 Thr Gly Thr Leu Lys Phe Cys Pro Leu Glu Lys Ala Gln Lys Leu Trp

Lys Glu Asn Pro Ser Glu Ile Tyr Pro Ile Met Asn Thr Thr Arg

135

```
150
                                        155
145
Thr Arg Leu Ala Leu Ile Ile Cys Asn Thr Glu Phe Gln His Leu Ser
               165
                                   170
Pro Arg Val Gly Ala Gln Val Asp Leu Arg Glu Met Lys Leu Leu
                                                   190
                               185
           180
Glu Asp Leu Gly Tyr Thr Val Lys Val Lys Glu Asn Leu Thr Ala Leu
                           200
                                               205
Glu Met Val Lys Glu Val Lys Glu Phe Ala Ala Cys Pro Glu His Lys
                       215
                                            220
Thr Ser Asp Ser Thr Phe Leu Val Phe Met Ser His Gly Ile Gln Glu
                                        235
                   230
Gly Ile Cys Gly Thr Thr Tyr Ser Asn Glu Val Ser Asp Ile Leu Lys
                245
                                    250
Val Asp Thr Ile Phe Gln Met Met Asn Thr Leu Lys Cys Pro Ser Leu
                                265
Lys Asp Lys Pro Lys Val Ile Ile Gln Ala Cys Arg Gly Glu Lys
        275
                            280
                                                285
Gln Gly Val Val Leu Leu Lys Asp Ser Val Arg Asp Ser Glu Glu Asp
                        295
Phe Leu Thr Asp Ala Ile Phe Glu Asp Asp Gly Ile Lys Lys Ala His
                    310
                                        315
Ile Glu Lys Asp Phe Ile Ala Phe Cys Ser Ser Thr Pro Asp Asn Val
                325
                                    330
Ser Trp Arg His Pro Val Arg Gly Ser Leu Phe Ile Glu Ser Leu Ile
                                345
            340
Lys His Met Lys Glu Tyr Ala Trp Ser Cys Asp Leu Glu Asp Ile Phe
                            360
                                                365
        355
Arg Lys Val Arg Phe Ser Phe Glu Gln Pro Glu Phe Arg Leu Gln Met
                        375
                                            380
Pro Thr Ala Asp Arg Val Thr Leu Thr Lys Arg Phe Tyr Leu Phe Pro
                    390
                                        395
Gly His
<210> 15
<211> 4
<212> PRT
<213> Artificial Sequence
<220>
<221> VARIANT
<222> 3
<223> Xaa= Ala, His, Gln, Lys, Phe, Cha, or Asp.
<223> Designed Peptide
<400> 15
Tyr Val Xaa Asp
<210> 16
<211> 4
<212> PRT
<213> Artificial Sequence
```

<220>

<223> Designed Peptide

```
<221> VARIANT
<222> 1,4
<223> Xaa at position 1 is acetylated Tyr.
                                             Xaa at
      position 4 is Asp aldehyde.
<400> 16
Xaa Val Ala Xaa
<210> 17
<211> 4
<212> PRT
<213> Artificial Sequence
<220>
<223> Designed Peptide
<400> 17
Tyr Val Ala Asp
<210> 18
<211> 4
<212> PRT
<213> Artificial Sequence
<220>
<221> VARIANT
<222> 1,2, 4
<223> Xaa at position 1 is acetylated Tyr. Xaa at
      position 2 is D-Ala. Xaa at position 4 is Asp
      aldehyde.
<223> Designed Peptide
<400> 18
Xaa Xaa Ala Xaa
1
<210> 19
<211> 4
<212> PRT
<213> Artificial Sequence
<220>
<223> Designed Peptide
<221> VARIANT
<222> 1,4
<223> Xaa at position 1 is acetylated Tyr. Xaa at
      position 4 is Asp aldehyde.
<400> 19
Xaa Val Lys Xaa
1
```

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<210> 20
<211> 354
<212> PRT
<213> Caenorhabditis elegans
<220>
<221> VARIANT
<222> 211, 254, 263, 279, 300, 317, 334, 337
<223> Xaa = Any Amino Acid
<400> 20
Arg Ser Arg Ser Arg Ala Leu His Ser Ser Asp Arg His Asn
                                    10
Tyr Ser Ser Pro Pro Val Asn Ala Phe Pro Ser Gln Pro Ser Ser Ala
            20
                                25
Asn Ser Ser Phe Thr Gly Cys Ser Ser Leu Gly Tyr Ser Ser Ser Arg
                            40
Asn Arg Ser Phe Ser Lys Ala Ser Gly Pro Thr Gln Tyr Ile Phe His
                        55
Glu Glu Asp Met Asn Phe Val Asp Ala Pro Thr Ile Ser Arg Val Phe
                    70
                                        75
Asp Glu Lys Thr Met Tyr Arg Asn Phe Ser Ser Pro Arg Gly Met Cys
                85
                                    90
Leu Ile Ile Asn Asn Glu His Phe Glu Gln Met Pro Thr Arg Asn Gly
            100
                                105
Thr Lys Ala Asp Lys Asp Asn Leu Thr Asn Leu Phe Arg Cys Met Gly
                            120
                                                125
       115
Tyr Thr Val Ile Cys Lys Asp Asn Leu Thr Gly Arg Gly Met Leu Leu
                                            140
                        135
Thr Ile Arg Asp Phe Ala Lys His Glu Ser His Gly Asp Ser Ala Ile
                    150
                                        155
Leu Val Ile Leu Ser His Gly Glu Glu Asn Val Ile Ile Gly Val Asp
                165
                                    170
Asp Ile Pro Ile Ser Thr His Glu Ile Tyr Asp Leu Leu Asn Ala Ala
                                185
Asn Ala Pro Arg Leu Ala Asn Lys Pro Lys Ile Val Phe Val Gln Ala
       195
                            200
Cys Arg Xaa Glu Arg Arg Asp Asn Gly Phe Pro Val Leu Asp Ser Val
                        215
                                            220
Asp Gly Val Pro Ala Phe Leu Arg Arg Gly Trp Asp Asn Arg Asp Gly
                                        235
                   230
Pro Leu Phe Asn Phe Leu Gly Cys Val Arg Pro Gln Val Xaa Gln Val
                                    250
               245
Trp Arg Lys Lys Pro Ser Xaa Ala Asp Ile Leu Ile Arg Tyr Ala Thr
                                                    270
           260
                               265
Thr Ala Gln Tyr Val Ser Xaa Arg Asn Ser Ala Arg Gly Ser Trp Phe
       275
                            280
                                                285
Ile Gln Ala Val Cys Glu Val Phe Ser Thr His Xaa Lys Asp Met Asp
                        295
                                            300
Val Val Glu Leu Leu Thr Glu Val Asn Lys Lys Val Xaa Cys Gly Phe
                   310
                                       315
Gln Thr Ser Gln Gly Ser Asn Ile Leu Lys Gln Met Pro Xaa Met Thr
                                    330
Xaa Arg Leu Leu Lys Lys Phe Tyr Phe Trp Pro Glu Ala Arg Asn Ser
                                345
Ala Val
```

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<210> 21
<211> 131
<212> PRT
<213> Caenorhabditis elegans
<220>
<221> VARIANT
<222> 31, 40, 56, 77, 94, 111, 114
<223> Xaa = Any Amino Acid
<400> 21
Val Asp Gly Val Pro Ala Phe Leu Arg Arg Gly Trp Asp Asn Arg Asp
                                    10
Gly Pro Leu Phe Asn Phe Leu Gly Cys Val Arg Pro Gln Val Xaa Gln
                                25
Val Trp Arg Lys Lys Pro Ser Xaa Ala Asp Ile Leu Ile Arg Tyr Ala
Thr Thr Ala Gln Tyr Val Ser Xaa Arg Asn Ser Ala Arg Gly Ser Trp
Phe Ile Gln Ala Val Cys Glu Val Phe Ser Thr His Xaa Lys Asp Met
                    70
                                        75
Asp Val Val Glu Leu Leu Thr Glu Val Asn Lys Lys Val Xaa Cys Gly
                                    90
                85
Phe Gln Thr Ser Gln Gly Ser Asn Ile Leu Lys Gln Met Pro Xaa Met
            100
                                105
Thr Xaa Arg Leu Leu Lys Lys Phe Tyr Phe Trp Pro Glu Ala Arg Asn
        115
                            120
Ser Ala Val
    130
<210> 22
<211> 223
<212> PRT
<213> Caenorhabditis elegans
<220>
<221> VARIANT
<222> 211
<223> Xaa = Any Amino Acid
<400> 22
Arg Ser Arg Ser Arg Ser Arg Ala Leu His Ser Ser Asp Arg His Asn
                                    10
Tyr Ser Ser Pro Pro Val Asn Ala Phe Pro Ser Gln Pro Ser Ser Ala
                                25
Asn Ser Ser Phe Thr Gly Cys Ser Ser Leu Gly Tyr Ser Ser Ser Arg
                            40
Asn Arg Ser Phe Ser Lys Ala Ser Gly Pro Thr Gln Tyr Ile Phe His
Glu Glu Asp Met Asn Phe Val Asp Ala Pro Thr Ile Ser Arg Val Phe
Asp Glu Lys Thr Met Tyr Arg Asn Phe Ser Ser Pro Arg Gly Met Cys
                                    90
Leu Ile Ile Asn Asn Glu His Phe Glu Gln Met Pro Thr Arg Asn Gly
                                105
Thr Lys Ala Asp Lys Asp Asn Leu Thr Asn Leu Phe Arg Cys Met Gly
                           120
Tyr Thr Val Ile Cys Lys Asp Asn Leu Thr Gly Arg Gly Met Leu Leu
```

```
135
Thr Ile Arg Asp Phe Ala Lys His Glu Ser His Gly Asp Ser Ala Ile
                   150
                                        155
Leu Val Ile Leu Ser His Gly Glu Glu Asn Val Ile Ile Gly Val Asp
                165
                                    170
Asp Ile Pro Ile Ser Thr His Glu Ile Tyr Asp Leu Leu Asn Ala Ala
            180
                                185
Asn Ala Pro Arg Leu Ala Asn Lys Pro Lys Ile Val Phe Val Gln Ala
                            200
Cys Arg Xaa Glu Arg Arg Asp Asn Gly Phe Pro Val Leu Asp Ser
    210
                        215
<210> 23
<211> 294
<212> PRT
<213> Homo sapiens
<220>
<221> VARIANT
<222> 175, 177, 214, 230, 251, 280, 283
<223> Xaa = Any Amino Acid
<400> 23
Phe Pro Ala Pro Gln Ala Val Gln Asp Asn Pro Ala Met Pro Thr Ser
 1
                                    10
Ser Gly Ser Glu Gly Asn Val Lys Leu Cys Ser Leu Glu Glu Ala Gln
            20
Arg Ile Trp Lys Gln Lys Ser Ala Glu Ile Tyr Pro Ile Met Asp Lys
                             40
Ser Ser Arg Thr Arg Leu Ala Leu Ile Ile Cys Asn Glu Glu Phe Asp
Ser Ile Pro Arg Arg Thr Gly Ala Glu Val Asp Ile Thr Gly Met Thr
                    70
                                         75
Met Leu Leu Gln Asn Leu Gly Tyr Ser Val Asp Val Lys Lys Asn Leu
                                    90
                85
Thr Ala Ser Asp Met Thr Thr Glu Leu Glu Ala Phe Ala His Arg Pro
                                105
Glu His Lys Thr Ser Asp Ser Thr Phe Leu Val Phe Met Ser His Gly
                                                 125
                            120
        115
Ile Arg Glu Gly Ile Cys Gly Lys Lys His Ser Glu Gln Val Pro Asp
                        135
                                             140
Ile Leu Gln Leu Asn Ala Ile Phe Asn Met Leu Asn Thr Lys Asn Cys
                                        155
                    150
Pro Ser Leu Lys Asp Lys Pro Lys Val Ile Ile Ile Gln Ala Xaa Arg
               165
                                    170
Xaa Asp Ser Pro Gly Val Val Trp Phe Lys Asp Ser Val Gly Val Ser
           180
                                185
                                                    190
Gly Asn Leu Ser Leu Pro Thr Thr Glu Glu Phe Glu Asp Asp Ala Ile
                            200
                                                205
Lys Lys Ala His Ile Xaa Lys Asp Phe Ile Ala Phe Cys Ser Ser Thr
                        215
                                             220
Pro Asp Asn Val Ser Xaa Arg His Pro Thr Met Gly Ser Val Phe Ile
                    230
                                        235
·Gly Arg Leu Ile Glu His Met Gln Glu Tyr Xaa Cys Ser Cys Asp Val
                                    250
Glu Glu Ile Phe Arg Lys Val Arg Phe Ser Phe Glu Gln Pro Asp Gly
                                265
```

Arg Ala Gln Met Pro Thr Thr Xaa Arg Val Xaa Leu Thr Arg Cys Phe

```
275 280 285
```

Tyr Leu Phe Pro Gly His 290

<210> 24

<211> 107

<212> PRT

<213> Homo sapiens

<220>

<221> VARIANT

<222> 27, 43, 64, 93, 96

<223> Xaa = Any Amino Acid

<400> 24

Ser Val Gly Val Ser Gly Asn Leu Ser Leu Pro Thr Thr Glu Glu Phe 1 5 10 15

Glu Asp Asp Ala Ile Lys Lys Ala His Ile Xaa Lys Asp Phe Ile Ala 20 25 30

Phe Cys Ser Ser Thr Pro Asp Asn Val Ser Xaa Arg His Pro Thr Met 35 40 45

Gly Ser Val Phe Ile Gly Arg Leu Ile Glu His Met Gln Glu Tyr Xaa 50 55 60

Cys Ser Cys Asp Val Glu Glu Ile Phe Arg Lys Val Arg Phe Ser Phe
65 70 75 80

Glu Gln Pro Asp Gly Arg Ala Gln Met Pro Thr Thr Xaa Arg Val Xaa 85 90 95

Leu Thr Arg Cys Phe Tyr Leu Phe Pro Gly His

<210> 25

<211> 187

<212> PRT

<213> Homo sapiens

<220>

<221> VARIANT

<222> 175, 177

<223> Xaa = Any Amino Acid

<400> 25

Phe Pro Ala Pro Gln Ala Val Gln Asp Asn Pro Ala Met Pro Thr Ser

Ser Gly Ser Glu Gly Asn Val Lys Leu Cys Ser Leu Glu Glu Ala Gln 20 25 30

Arg Ile Trp Lys Gln Lys Ser Ala Glu Ile Tyr Pro Ile Met Asp Lys 35 40 45

Ser Ser Arg Thr Arg Leu Ala Leu Ile Ile Cys Asn Glu Glu Phe Asp 50 55 60

Ser Ile Pro Arg Arg Thr Gly Ala Glu Val Asp Ile Thr Gly Met Thr 65 70 75 80

Met Leu Leu Gln Asn Leu Gly Tyr Ser Val Asp Val Lys Lys Asn Leu 85 90 95

Thr Ala Ser Asp Met Thr Thr Glu Leu Glu Ala Phe Ala His Arg Pro
100 105 110

Glu His Lys Thr Ser Asp Ser Thr Phe Leu Val Phe Met Ser His Gly
115 120 125

```
Ile Arg Glu Gly Ile Cys Gly Lys Lys His Ser Glu Gln Val Pro Asp
                       135
Ile Leu Gln Leu Asn Ala Ile Phe Asn Met Leu Asn Thr Lys Asn Cys
                  150
                                       155
Pro Ser Leu Lys Asp Lys Pro Lys Val Ile Ile Gln Ala Xaa Arg
               165
                                   170
Xaa Asp Ser Pro Gly Val Val Trp Phe Lys Asp
           180
<210> 26
<211> 172
<212> PRT
<213> Murine
<220>
<221> VARIANT
<222> 118
<223> Xaa = Any Amino Acid
<400> 26
Met Leu Thr Val Gln Val Tyr Arg Thr Ser Gln Lys Cys Ser Ser Ser
1
                                   10
Lys His Val Val Glu Val Leu Leu Asp Pro Leu Gly Thr Ser Phe Cys
           20
                               25
Ser Leu Leu Pro Pro Pro Leu Leu Tyr Glu Thr Asp Arg Gly Val
       35
                            40
Asp Gln Gln Asp Gly Lys Asn His Thr Gln Ser Pro Gly Cys Glu Glu
                        55
Ser Asp Ala Gly Lys Glu Glu Leu Met Lys Met Arg Leu Pro Thr Arg
Ser Asp Met Ile Cys Gly Tyr Ala Cys Leu Lys Gly Asn Ala Ala Met
               85
                                   90
Arg Asn Thr Lys Arg Gly Ser Trp Tyr Ile Glu Ala Leu Thr Gln Val
                               105
                                                   110
           100
Phe Ser Glu Arg Ala Xaa Cys Asp Met His Val Ala Asp Met Leu Val
                           120
                                               125
Lys Val Asn Ala Leu Ile Lys Glu Arg Glu Gly Tyr Ala Pro Gly Thr
                       135
                                           140
Glu Phe His Arg Cys Lys Glu Met Ser Glu Tyr Cys Ser Thr Leu Cys
                  150
                                       155
Gln Gln Leu Tyr Leu Phe Pro Gly Tyr Pro Pro Thr
<210> 27
<211> 172
<212> PRT
<213> Murine
<220>
<221> VARIANT
<222> 118
<223> Xaa = Any Amino Acid
<400> 27
Met Leu Thr Val Gln Val Tyr Arg Thr Ser Gln Lys Cys Ser Ser Ser
                                   10
```

Lys His Val Val Glu Val Leu Leu Asp Pro Leu Gly Thr Ser Phe Cys

20 25 Ser Leu Leu Pro Pro Pro Leu Leu Leu Tyr Glu Thr Asp Arg Gly Val 40 Asp Gln Gln Asp Gly Lys Asn His Thr Gln Ser Pro Gly Cys Glu Glu 55 60 Ser Asp Ala Gly Lys Glu Glu Leu Met Lys Met Arg Leu Pro Thr Arg 70 75 Ser Asp Met Ile Cys Gly Tyr Ala Cys Leu Lys Gly Asn Ala Ala Met 85 90 Arg Asn Thr Lys Arg Gly Ser Trp Tyr Ile Glu Ala Leu Thr Gln Val 105 Phe Ser Glu Arg Val Xaa Cys Asp Met His Val Ala Asp Met Leu Val 120 Lys Val Asn Ala Leu Ile Lys Glu Arg Glu Gly Tyr Ala Pro Gly Thr 135 140 Glu Phe His Arg Cys Lys Glu Met Ser Glu Tyr Cys Ser Thr Leu Cys 150 155 Gln Gln Leu Tyr Leu Phe Pro Gly Tyr Pro Pro Thr 165

<210> 28 <211> 451 <212> PRT <213> Murine

<400> 28 Met Ala Ala Pro Ser Gly Arg Ser Gln Ser Ser Leu His Arg Lys Gly 10 Leu Met Ala Ala Asp Arg Arg Ser Arg Ile Leu Ala Val Cys Gly Met 2.5 His Pro Asp His Gln Glu Thr Leu Lys Lys Asn Arg Val Val Leu Ala 35 Lys Gln Leu Leu Ser Glu Leu Leu Glu His Leu Leu Glu Lys Asp 55 Ile Ile Thr Leu Glu Met Arg Glu Leu Ile Gln Ala Lys Gly Gly Ser 75 70 Phe Ser Gln Asn Val Glu Leu Asn Leu Leu Pro Lys Arg Gly Pro Gln 85 90 Ala Phe Asp Ala Phe Cys Glu Ala Leu Arg Glu Thr Arg Gln Gly His 100 105 110 Leu Glu Asp Leu Leu Thr Thr Leu Ser Asp Ile Gln His Val Leu 120 125 Pro Pro Leu Ser Cys Asp Tyr Asp Thr Ser Leu Pro Phe Ser Val Cys 135 140 Glu Ser Cys Pro Pro His Lys Gln Leu Arg Leu Ser Thr Asp Ala Thr 150 155 Glu His Ser Leu Asp Asn Gly Asp Gly Pro Pro Cys Leu Leu Val Lys 170 Pro Cys Thr Pro Glu Phe Tyr Gln Ala His Tyr Gln Leu Ala Tyr Arg 185 Leu Gln Ser Gln Pro Arg Gly Leu Ala Leu Val Leu Ser Asn Val His 200 Phe Thr Gly Glu Lys Asp Leu Glu Phe Arg Ser Gly Gly Asp Val Asp 215 220 His Thr Thr Leu Val Thr Leu Phe Lys Leu Leu Gly Tyr Asn Val His 230 235 Val Leu His Asp Gln Thr Ala Gln Glu Met Gln Glu Lys Leu Gln Asn

Phe Ala Gln Leu Pro Ala His Arg Val Thr Asp Ser Cys Val Val Ala 260 265 Leu Leu Ser His Gly Val Glu Gly Gly Ile Tyr Gly Val Asp Gly Lys 280 Leu Leu Gln Leu Gln Glu Val Phe Arg Leu Phe Asp Asn Ala Asn Cys 295 300 Pro Ser Leu Gln Asn Lys Pro Lys Met Phe Phe Ile Gln Ala Cys Arg 310 315 Gly Asp Glu Thr Asp Arg Gly Val Asp Gln Gln Asp Gly Lys Asn His 325 330 Thr Gln Ser Pro Gly Cys Glu Glu Ser Asp Ala Gly Lys Glu Glu Leu 340 345 350 Met Lys Met Arg Leu Pro Thr Arg Ser Asp Met Ile Cys Gly Tyr Ala 355 360 365 Cys Leu Lys Gly Asn Ala Ala Met Arg Asn Thr Lys Arg Gly Ser Trp 375 380 Tyr Ile Glu Ala Leu Thr Gln Val Phe Ser Glu Arg Ala Cys Asp Met 390 395 His Val Ala Asp Met Leu Val Lys Val Asn Ala Leu Ile Lys Glu Arg 405 410 Glu Gly Tyr Ala Pro Gly Thr Glu Phe His Arg Cys Lys Glu Met Ser 425 Glu Tyr Cys Ser Thr Leu Cys Gln Gln Leu Tyr Leu Phe Pro Gly Tyr 435 Pro Pro Thr 450

<210> 29

<211> 503

<212> PRT

<213> Caenorhabditis elegans

<400> 29

Met Met Arg Gln Asp Arg Arg Ser Leu Leu Glu Arg Asn Ile Met Met Phe Ser Ser His Leu Lys Val Asp Glu Ile Leu Glu Val Leu Ile Ala Lys Gln Val Leu Asn Ser Asp Asn Gly Asp Met Ile Asn Ser Cys Gly Thr Val Arg Glu Lys Arg Arg Glu Ile Val Lys Ala Val Gln Arg Arg 55 Gly Asp Val Ala Phe Asp Ala Phe Tyr Asp Ala Leu Arg Ser Thr Gly 70 75 His Glu Gly Leu Ala Glu Val Leu Glu Pro Leu Ala Arg Ser Val Asp 90 Ser Asn Ala Val Glu Phe Glu Cys Pro Met Ser Pro Ala Ser His Arg 105 Arg Ser Arg Ala Leu Ser Pro Ala Gly Tyr Thr Ser Pro Thr Arg Val 120 125 His Arg Asp Ser Val Ser Ser Val Ser Ser Phe Thr Ser Tyr Gln Asp 135 140 Ile Tyr Ser Arg Ala Arg Ser Arg Ser Arg Ser Arg Ala Leu His Ser 150 155 Ser Asp Arg His Asn Tyr Ser Ser Pro Pro Val Asn Ala Phe Pro Ser 165 170 Gln Pro Ser Ser Ala Asn Ser Ser Phe Thr Gly Cys Ser Ser Leu Gly 185 Tyr Ser Ser Ser Arg Asn Arg Ser Phe Ser Lys Ala Ser Gly Pro Thr

```
200
                                                205
       195
Gln Tyr Ile Phe His Glu Glu Asp Met Asn Phe Val Asp Ala Pro Thr
                      215
                                     220
Ile Ser Arg Val Phe Asp Glu Lys Thr Met Tyr Arg Asn Phe Ser Ser
                   230
                                       235
Pro Arg Gly Met Cys Leu Ile Ile Asn Asn Glu His Phe Glu Gln Met
               245
                                   250
Pro Thr Arg Asn Gly Thr Lys Ala Asp Lys Asp Asn Leu Thr Asn Leu
                               265
Phe Arg Cys Met Gly Tyr Thr Val Ile Cys Lys Asp Asn Leu Thr Gly
       275
                           280
Arg Gly Met Leu Leu Thr Ile Arg Asp Phe Ala Lys His Glu Ser His
                       295
                                           300
Gly Asp Ser Ala Ile Leu Val Ile Leu Ser His Gly Glu Glu Asn Val
                   310
                                        315
Ile Ile Gly Val Asp Asp Ile Pro Ile Ser Thr His Glu Ile Tyr Asp
               325
                                    330
Leu Leu Asn Ala Ala Asn Ala Pro Arg Leu Ala Asn Lys Pro Lys Ile
           340
                                345
Val Phe Val Gln Ala Cys Arg Gly Glu Arg Arg Asp Asn Gly Phe Pro
                            360
Val Leu Asp Ser Val Asp Gly Val Pro Ala Phe Leu Arg Arg Gly Trp
                        375
                                           380
Asp Asn Arg Asp Gly Pro Leu Phe Asn Phe Leu Gly Cys Val Arg Pro
                    390
                                        395
Gln Val Gln Gln Val Trp Arg Lys Lys Pro Ser Gln Ala Asp Ile Leu
                                    410
Ile Arg Tyr Ala Thr Thr Ala Gln Tyr Val Ser Trp Arg Asn Ser Ala
                                425
           420
Arg Gly Ser Trp Phe Ile Gln Ala Val Cys Glu Val Phe Ser Thr His
       435
                            440
Ala Lys Asp Met Asp Val Val Glu Leu Leu Thr Glu Val Asn Lys Lys
                       455
                                           460
Val Ala Cys Gly Phe Gln Thr Ser Gln Gly Ser Asn Ile Leu Lys Gln
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                   470
Met Pro Glu Met Thr Ser Arg Leu Leu Lys Lys Phe Tyr Phe Trp Pro
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Glu Ala Arg Asn Ser Ala Val
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<211> 404

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<213> Homo sapiens

<400> 30

 Met Ala Asp Lys Val
 Leu Lys Glu Lys Arg Lys Leu Phe Ile Arg Ser

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 Met Gly Glu Gly Thr Ile Asn Gly Leu Leu Asp Glu Leu Leu Gln Thr

 20
 25

 Arg Val Leu Asn Lys Glu Glu Met Glu Lys Val Lys Arg Glu Asn Ala

 35
 40

 40
 45

 Thr Val Met Asp Lys Thr Arg Ala Leu Ile Asp Ser Val Ile Pro Lys

 50
 55

 60

 Gly Ala Gln Ala Cys Gln Ile Cys Ile Thr Tyr Ile Cys Glu Glu Asp

 65
 70

 75
 80

 Ser Tyr Leu Ala Gly Thr Leu Gly Leu Ser Ala Asp Gln Thr Ser Gly

 85

Asn Tyr Leu Asn Met Gln Asp Ser Gln Gly Val Leu Ser Ser Phe Pro Ala Pro Gln Ala Val Gln Asp Asn Pro Ala Met Pro Thr Ser Ser Gly Ser Glu Gly Asn Val Lys Leu Cys Ser Leu Glu Glu Ala Gln Arg Ile Trp Lys Gln Lys Ser Ala Glu Ile Tyr Pro Ile Met Asp Lys Ser Ser Arg Thr Arg Leu Ala Leu Ile Ile Cys Asn Glu Glu Phe Asp Ser Ile Pro Arg Arg Thr Gly Ala Glu Val Asp Ile Thr Gly Met Thr Met Leu Leu Gln Asn Leu Gly Tyr Ser Val Asp Val Lys Lys Asn Leu Thr Ala Ser Asp Met Thr Thr Glu Leu Glu Ala Phe Ala His Arg Pro Glu His Lys Thr Ser Asp Ser Thr Phe Leu Val Phe Met Ser His Gly Ile Arg Glu Gly Ile Cys Gly Lys Lys His Ser Glu Gln Val Pro Asp Ile Leu Gln Leu Asn Ala Ile Phe Asn Met Leu Asn Thr Lys Asn Cys Pro Ser Leu Lys Asp Lys Pro Lys Val Ile Ile Ile Gln Ala Cys Arg Gly Asp Ser Pro Gly Val Val Trp Phe Lys Asp Ser Val Gly Val Ser Gly Asn Leu Ser Leu Pro Thr Thr Glu Glu Phe Glu Asp Asp Ala Ile Lys Lys Ala His Ile Glu Lys Asp Phe Ile Ala Phe Cys Ser Ser Thr Pro Asp Asn Val Ser Trp Arg His Pro Thr Met Gly Ser Val Phe Ile Gly Arg Leu Ile Glu His Met Gln Glu Tyr Ala Cys Ser Cys Asp Val Glu Glu Ile Phe Arg Lys Val Arg Phe Ser Phe Glu Gln Pro Asp Gly Arg Ala Gln Met Pro Thr Thr Glu Arg Val Thr Leu Thr Arg Cys Phe Tyr Leu Phe Pro Gly His